

In the Claims

Please amend the claims to read as follows:

1. (currently amended) A method for the treatment of a tumor in a mammal, ~~wherein the~~ comprising the steps of a) determining that said tumor is characterized by the overexpression of an ErbB2 receptor, b) determining that said tumor ~~and does not respond, or responds poorly, to treatment with an anti-ErbB2 antibody, and c) comprising~~ administering to the mammal a therapeutically effective amount of a conjugate of the anti-ErbB2 antibody with a maytansinoid.

2. (original) The method of claim 1 wherein the mammal is human.

4. (previously presented) The method of claim 1 wherein the anti-ErbB2 antibody is a growth inhibitory antibody.

5. (previously presented) The method of claim 1 wherein the anti-ErbB2 antibody induces cell death.

6. (previously presented) The method of claim 1 wherein the anti-ErbB2 antibody induces apoptosis.

8. (previously presented) The method of claim 1 wherein the tumor is cancer.

9. (original) The method of claim 8 wherein the cancer is selected from the group consisting of breast, ovarian, stomach, endometrial, salivary gland, lung, kidney, colon, colorectal, thyroid, pancreatic, prostate and bladder cancer.

10. (original) The method of claim 9 wherein the cancer is breast cancer.

11. (original) The method of claim 10 wherein the breast cancer overexpresses ErbB2 at a 2+ level or more.

12. (original) The method of claim 11 wherein the breast cancer overexpresses ErbB2 at a 3+ level.

13. (original) The method of claim 12 wherein the breast cancer is a metastatic breast cancer.

14. (currently amended) The method of claim 12 wherein the antibody has a biological characteristic of a 4D5 monoclonal antibody such that the antibody shows a growth inhibitory effect on ErbB2 overexpressing cells in a manner that is dependent on the ErbB2 expression level and/or blocks binding of monoclonal antibody 4D5 to ErbB2.

15. (original) The method of claim 14 wherein the antibody binds essentially the same epitope as a 4D5 monoclonal antibody.

16. (original) The method of claim 14 wherein the antibody is the monoclonal antibody 4D5 (ATCC CRL 10463).

17. (original) The method of claim 14 wherein the antibody is humanized.

18. (previously presented) The method of claim 17 wherein the antibody is selected from the group consisting of humanized antibodies huMAb4D5-1, huMAb4D5-2, huMAb4D5-3, huMAb4D5-4, huMAb4D5-5, huMAb4D5-6, huMAb4D5-7 and huMAb4D5-8.

19. (previously presented) The method of claim 18 wherein the antibody is humanized antibody huMAb4D5-8.

20. (previously presented) The method of claim 1 wherein the antibody is an antibody fragment.

21. (original) The method of claim 20 wherein the antibody fragment is selected from the group consisting of a Fab, Fab', F(ab')₂, F_v fragment, diabody, linear antibody, and single-chain antibody molecule.

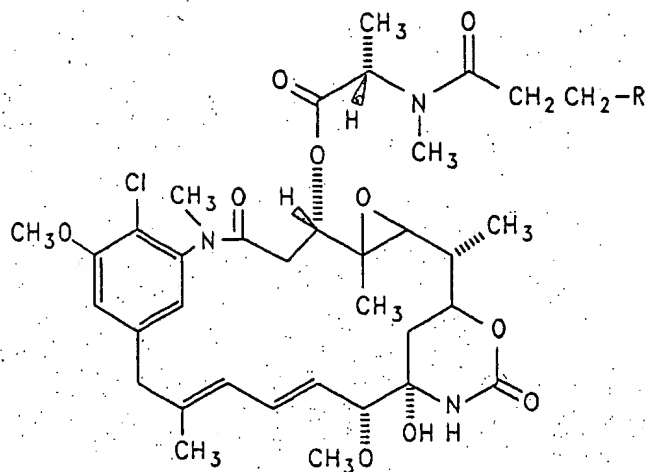
22. (previously presented) The method of claim 1 wherein the maytansinoid is maytansine.

23. (original) The method of claim 1 wherein the maytansinoid is maytansinol.

24. (original) The method of claim 1 wherein the maytansinoid is a maytansinol ester.

25. (original) The method of claim 24 wherein the maytansinoid is a C-3 ester of maytansinol.

26. (currently amended) The method of claim 25 wherein the maytansinoid is DM1 having the structure



wherein R is capable of forming a chemical bond with a linker.

27. (previously presented) The method of claim 1 wherein the antibody and maytansinoid are conjugated by a bispecific chemical linker.

28. (original) The method of claim 27 wherein said chemical linker is N-succinimidyl-4-(2-pyridylthio)propanoate (SPDP) or N-succinimidyl-4-(2-pyridylthio)pentanoate (SPP).

29. (previously presented) The method of claim 1 wherein the antibody and maytansinoid are conjugated by a linking group selected from the group consisting of a disulfide, thioether, acid labile, photolabile, peptidase labile, and esterase labile group.

30. (original) The method of claim 29 wherein the linking group is a disulfide or a thioether group.
31. (original) The method of claim 30 wherein the linking group is a disulfide group.
32. (original) The method of claim 1 wherein the conjugate comprises 1 to about 10 maytansinoid molecules per antibody molecule.
33. (original) The method of claim 32 wherein the conjugate comprises from about 3 to about 5 maytansinoid molecules per antibody molecule.
34. (previously presented) The method of claim 1 further comprising the administration of a second antibody which binds ErbB2.
35. (original) The method of claim 34 wherein the second antibody comprises monoclonal antibody 2C4 or humanized 2C4.
36. (previously presented) The method of claim 34 wherein the second antibody is humanized antibody, huMAb4D5-8.
37. (original) The method of claim 1 wherein treatment with the conjugate is followed by treatment with an unconjugated anti-ErbB antibody.
38. (original) The method of claim 32 wherein the conjugate is administered weekly at a dose of 0.1 to 10 mg/kg body weight.
39. (original) The method of claim 38 wherein said administration is followed by a dose of 0.3 mg/kg body weight approximately 10 weeks later.
40. (original) The method of claim 33 wherein the conjugate is administered weekly at a dose of 1 to 3 mg/kg body weight.
41. (original) The method of claim 40 wherein said administration is followed by a dose of 0.3 mg/kg body weight approximately 10 weeks later.

42. (previously presented) The method of claim 1 wherein the conjugate is administered weekly at a dose of 0.1 to 5 mg/kg body weight for 4 to 6 weeks, followed by maintenance treatment with unconjugated anti-ErbB2 antibody.

43. (previously presented) The method of claim 42 wherein the unconjugated antibody is humanized antibody huMAb4D5-8 or humanized 2C4.

44. (original) The method of claim 34 wherein said second antibody is conjugated with a cytotoxic agent.

45. (original) The method of claim 44 wherein the cytotoxic agent is a maytansinoid.

46. (previously presented) The method of claim 1 wherein said treatment has an improved objective response rate compared to treatment with huMAb4D5-8 alone.

47. (previously presented) The method of claim 1 wherein said treatment has a longer duration of response than treatment with huMAb4D5-8 alone.

48. (previously presented) The method of claim 1 wherein said treatment results in increased survival of the mammal treated compared with treatment with huMAb4D5-8 alone.